

incorporated by reference. In brief, the present technology describes the novel and pharmaceutically relevant, and therefore commercially valuable, "product" of a patented invention.

SUMMARY OF THE INVENTION

The human genome has been sequenced. For as long as the human species endures virtually all future human drugs (with the notable exception of antibiotics) will directly or indirectly interact with products encoded by one or more products encoded by this finite subset of genetic information. The remaining and substantially more scientifically daunting challenge is to conclusively identify those portions of the genome that actually encode proteins, and then define the physiological functions of these proteins. For a variety of reasons the mouse has emerged as the animal system that will predominantly be employed to discover a given gene's role in mammalian physiology. The present invention derives from the discovery of a high throughput method of generating clonal lines of mutated murine ES cells.

The described ES cells are totipotent. Consequently, the described ES cells can be cultured and genetically altered *in vitro* and then used to produce mice (via microinjection of the ES cells to generate chimeric mice and subsequent breeding steps) having a genetically engineered mutation in a specific gene— in this case the genetic locus that encodes the exon data presented in SEQ ID NO:393. The resulting "knockout" mice can then be subject to a medical work-up to determine the function of the corresponding gene product (or absence thereof) in mammalian physiology. As such, the mutated ES cells broadly described in the present application will likely provide many discoveries of human gene function (via the study of the effects of the corresponding murine gene in mutated/"knockout" mice). The described collection of mutated murine ES cell clones represent a subset of a larger collection of over two hundred thousand ES cell clones that have been identified using a high throughput gene trapping system.

The elected genetically engineered ES cell species presently at issue mutates the murine genetic locus encoding SEQ ID NO:393 and thus *specifically* allows for the discovery of the function of a specific gene— in this case the murine ortholog of the human neurexin II gene within the broader context of mammalian physiology.